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Award Number: DAMD17-98-1-8349

TITLE: ETACT-An Innovative Approach to Scintimammography

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REPORT DATE: July 2000

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

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REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 074-0188

1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	July 2000	Annual (1 Jul 99 - 30 Jun 00)

4. TITLE AND SUBTITLE
ETACT-An Innovative Approach to Scintimammography

5. FUNDING NUMBERS
DAMD17-98-1-8349

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8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSORING / MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES
Report contains color photos

12a. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for public release; distribution unlimited

12b. DISTRIBUTION CODE

13. ABSTRACT ***(Maximum 200 Words)***

This project investigates the use of a novel approach to scintimammography (SMM) known as emission tuned aperture computed tomography (ETACT). In ETACT, a series of projections of the radionuclide distribution in the breast are acquired with fiducial markers. These data are reconstructed into tomographic slices. The hypothesis of this project is that ETACT will significantly increase the diagnosis accuracy of SMM, and can be applied in a simple, flexible and practical manner. We have developed a simulation model for the acquisition process of ETACT and have used this tool to perform an evaluation of the aperture size appropriate for ETACT. It was determined that a 3 mm diameter aperture was optimal for ETACT. We performed a preliminary phantom evaluation with 3 tumor sizes (6, 8, 13 mm) and a 10:1 T/NT ratio. The 8 and 13 mm tumors were visible whereas the 6 mm was not. We will continue to work on our ETACT simulator to include attenuation and scatter. We will simulate ETACT data to evaluate projection number and divergence as a function of tumor size, location and T/NT ratio. We will further evaluate ETACT and compare it to planar and SPECT imaging through phantom studies. We will develop an ETACT clinical prototype of the procedure.

14. SUBJECT TERMS	15. NUMBER OF PAGES
Breast Cancer, scintimammography, tomography	21
	16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	Unlimited

NSN 7540-01-280-5500

Standard Form 298 (Rev. 2-89)
Prescribed by ANSI Std. Z39-18
298-102

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N/A In the conduct of research utilizing recombinant DNA, the investigator(s) adhered to the NIH Guidelines for Research Involving Recombinant DNA Molecules.

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Fredrick H Fry 7/27/00

PI - Signature Date

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Introduction

This project is investigating the use of a novel approach to scintimammography (SMM) known as emission tuned aperture computed tomography (ETACT). ETACT is based on the more general tuned aperture computed tomography (TACT) method used in radiography. TACT has been successfully applied in dentistry and its use in conventional mammography is currently being investigated. In ETACT, fiducial markers are placed around the object being imaged. A series of projection images are then acquired using a standard gamma camera with a pinhole (or other) collimator from any angle and at any distance, as long as all of the markers are within the field of view. The data are then reconstructed into a series of tomographic slices. This can be reconstructed easily on a PC. Thus TACT requires no expensive, dedicated hardware. The beauty of this approach is that, if successful, this method could be applied in practically every hospital in the US, almost immediately. The main hypothesis of this project is that the application of ETACT will significantly increase the diagnostic and prognostic accuracy of SMM, particularly for small, nonpalpable lesions, and that this innovative method can be applied in the clinic in a simple, flexible and practical manner. The specific aims of this research are as follows:

1. to develop and utilize a computer simulation model of ETACT to determine the optimal parameters for its application and to compare it to conventional SMM,
2. to utilize phantom data to further compare ETACT to conventional SMM, both planar and SPECT, and
3. to design a clinical ETACT prototype system that will then be used in a subsequent preliminary clinical investigation.

In this report, we will present our progress in further development of a computer simulation model of ETACT, the results from the use of such a model, and some preliminary phantom experiment results. We will discuss the changes in our approach that has been dictated by these preliminary results and present an outline for the remainder of this project.

Body of the Report

I. ETACT

In ETACT, one or more fiducial markers are placed about the patient's breast. A series of projection images are then acquired with a pinhole-collimated, gamma camera. We use pinhole collimation for three reasons. First, pinhole collimators are routinely available for most portable, gamma cameras, making this method a straightforward approach that can be applied in practically any hospital. Secondly, we plan to take advantage of the high resolution associated with pinhole collimation. For a typical pinhole collimator of length of 30 cm and pinhole diameter of 4 mm as well as an intrinsic spatial resolution of the detector of 3.5 mm, the system spatial resolution is approximately 5 mm compared to that of planar and SPECT imaging with a high resolution collimator of approximately 7 mm and 10 mm, respectively. Special inserts could also be made that would reduce the pinhole diameter from 4 to 2 mm improving the resolution to approximately 3 mm. Thirdly, the collimator sensitivity is inversely proportional to the square of the aperture-to-object distance whereas the sensitivity of a parallel hole collimator does not vary with collimator-to-object distance.

Consider the technique known as "tomosynthesis" (Grant 1972). In this case, the detector (the gamma camera crystal) is always oriented parallel to the tomographic plane of interest. Several projections are acquired such that all of the aperture (pinhole) locations are known, coplanar and parallel to the tomographic plane of interest. A series of tomographic planes can be reconstructed by appropriately shifting the projection data and adding them together. All reconstructed planes are parallel to the detector plane. Tomosynthesis has been shown to be a very simple and effective manner of generating tomographic data. However, it places many constraints on the acquired projection data, and the aperture locations for all of the projections must be known.

ETACT alleviates these geometric constraints by using the projected locations of a series of fiducial markers to obtain knowledge concerning each projection (Webber 1997). Consider the case where the detector is still coplanar and parallel to the tomographic plane of interest, but the actual location is not known. A fiducial marker whose location relative to the object is fixed is also imaged within each projection. Consider a reference plane whose location is the same as the aperture to detector distance, but whose location is opposite the detector (see Figure 1). If we overlay all of the

projections and add them, we are reconstructing the reference plane. If we determine the center of mass (COM) of the projected locations of the marker, shift all of the data such that projected location of the marker coincides with the COM and add the data together, we would reconstruct the plane that contains the fiducial marker and is parallel to the detector plane. If the projections are shifted by half that amount and added, then the plane that is half way between the marker and the reference plane is reconstructed. In this manner, any arbitrary plane can be reconstructed.

In the present implementation of ETACT, 5 markers are used, four of which are coplanar and one of which is not. The four coplanar markers are used to transform all of the acquired projections such that they appear to all have been acquired with the aperture in a common plane. The fifth marker is then used as described above to shift and add the projections to reconstruct the series of tomographic slices. It also has been demonstrated that this approach with the five fiducial markers can be used to reconstruct the data even if the detector in each projection is not always in the same plane. In summary, if we acquire a series of projection images using a set of 5 fiducial markers (4 coplanar and one out of plane), we can reconstruct the data into a series of tomographic slices, even if the location of neither the detector nor the aperture is known. It is also not necessary to have the detector in the same plane or at the same distance in each projection. Therefore, ETACT is a simple and flexible method of acquiring and processing tomographic data.

ETACT is a form of "blurring" tomography, that is, the activity that is not in the plane of interest is still present in the image, but it is blurred. Therefore, if there is a lot of out-of-plane activity, the contrast may be substantially blurred. In addition, very "hot" features (i.e. features with much more activity than the background) that are out-of-plane will lead to artifacts in the plane of interest. These artifacts can mimic small tumors in the ETACT images. The axial spatial resolution (i.e., the resolution in the direction normal to the tomographic plane of interest) is determined by the divergence of the acquired projection data. However, even in the best of cases, the axial spatial resolution is quite limited. We are currently investigating two approaches to address both of these limitations. The simplest approach is to "mask" the markers by either setting their pixel values to zero or to an average of neighboring pixels. Secondly, we can apply an iterative deconvolution since we can *a posteriori* determine the point spread function (PSF) of the system. We are currently evaluating these and other approaches.

II. Further Development of the ETACT Simulation Model

Last year, we reported the development of a computerized, simulation model of the acquisition of ETACT data. Due to the three-dimensional (3D) nature of this process, this model was developed using an Silicon Graphics, Inc. (SGI) workstation. We have migrated this application to Windows NT using the OpenGL libraries. The model currently allows you to define an arbitrary 3D object with a set of markers. The activity associated with each component can be defined. For example, we have defined a breast containing a tumor with 5 markers. The target-to-nontarget (T/NT) ratio of the tumor was 5:1. A projection from this simulated object is shown in Figure 2. In addition, the detector size and aperture-to-detector distance can be defined. Once the detector configuration and the object are defined, the detector can be moved interactively about object and simulated projections obtained. These data can be subsequently reconstructed with the standard, ETACT software. The projections are then blurred to the resolution and Poisson noise added that were consistent with the aperture size chosen. We have used this simulation model to evaluate the effect of the aperture size on contrast and signal-to-noise. Further investigations will consider the aperture to object distance, the number of projections and the angular disparity of the projections.

III. Evaluation of Aperture Size Through Simulation

We have performed an evaluation of the required aperture size for ETACT. We modeled the breast as a hemisphere with 15 cm diameter. The tumor was modeled as a sphere in the center of the breast. We considered 3 tumor sizes (5, 7.5 and 10 mm) and 2 target-to-nontarget (T/NT) ratios (5:1 and 10:1). Additional investgations also considered T/NT ratios of 12:1 and 15:1. Five markers (4 coplanar and one out-of-plane) were placed lateral to the breast. The detector was modeled as a gamma camera with a 50x50 cm filed-of-view. The aperture-to-detector distance was 25 cm. The aperture sizes (diameters) used were 1, 2, 3, 4, 5 and 6 mm. The aperture-to-object distance of approximately 15 cm was chosen such that the object, including the markers, took up the majority of the field of view. Using our projection simulator, we constructed 7 noiseless projections for each aperture size. The angular divergence was approximately +/- 20 degrees. One such projection is shown in Figure 2. Based on the calculated system spatial resolution of each pinhole, the projection data were blurred with a gaussian kernel. Based on the sensitivity of each pinhole size, Poisson

noise was added to each pixel. These data were then reconstructed using the standard TACT reconstruction software.

To evaluate these data, the slice through the middle of the tumor was visually selected and a region of interest (ROI) was drawn about the tumor and the maximum pixel value (Max) in the ROI was determined. A similar sized and shaped ROI was placed lateral to the tumor to evaluate the background activity. The mean pixel value (BKG) and the standard deviation (SD_{BKG}) in the background ROI were determined. The contrast (C) was calculated using the formula

$$C = \frac{Max - BKG}{BKG}$$

A detectability index referred to as the SNR was calculated by

$$SNR = \frac{C}{(SD_{BKG}/BKG)}$$

The results of this investigation are summarized in the following two graphs (Figures 3 and 4). In these figures, the nature of the tumor is indicated by S-TNT where S is the tumor size (in mm) and TNT is the T/NT ratio. For example, 5-10 indicates that this is the curve for a 5 mm tumor with a 10:1 T/NT ratio. In Figure 3, as the aperture size is reduced, the contrast improves. This is expected due to the improved resolution and the subsequent reduction in the partial volume effect. However, the sensitivity decreases with reduced aperture size leading to fewer photons being acquired and thus a noisier image. Therefore, Figure 4 shows that a 3 mm aperture is optimum with respect to the signal-to-noise ration (SNR) although not substantially better than the 4 mm aperture.

IV. Preliminary Phantom Experiment

A preliminary phantom experiment was performed to test the validity of the simulation study as well as the feasibility and practicality of the ETACT approach. For this experiment, we used the Data Spectrum breast phantom with 3 different tumor sizes (6, 8, 13 mm) with a 10:1 T/NT ratio. A portable gamma camera with a small field-of-view (30x30 cm) was used with a 4 mm pinhole

aperture. The aperture-to-tumor distance was approximately 15-20 cm. We used 5 markers (4 coplanar and one out of plane) as described earlier. These were point sources consisting of small amounts of Tc-99m placed at the ends of capillary tubes. The Data Spectrum phantom and our experimental set-up are shown in Figure 5. Seven projections were acquired for 5 minutes each. One projection from the 8 mm case is shown in Figure 6. The 5 markers are clearly visible in this projection. The tumor may be subtly visible.

These data were reconstructed into a series of slices using the standard ETACT algorithm as described earlier. The contrast, C, and the SNR as described earlier were determined for ETACT slice and compared to a planar acquisition. The results are shown below.

Tumor Size (mm)	Contrast	SNR
6	0.37	2.74
8	0.58	3.67
13	0.59	4.31

In these experiments, both the 8 mm and the 13 mm tumors were clearly visible after ETACT recnstruction, however the 6 mm tumor was not. This finding was consistent with our simulation results.

V. Summary of Preliminary Evaluation and Future Directions

These studies demonstrate the feasibility of the ETACT approach as well as the potential for improved lesion detectability. They also demonstrated the need to image at a substantial distance (upto 20 cm) in order to image the entire object including the markers. Imaging at such a distance leads to a substantial loss in the effectiveness of the pinhole collimator. The sensitivity of the pinhole collimator falls off as the inverse square of the object-to-aperture distance. Therefore, if we could reduce the aperture-to-object distance by a factor of 2, we would see a 4 fold increase in the number of counts and the noise level would decrease by half. Alternatively, we could either reduce the imaging time or improve the spatial resolution by using a smaller aperture size. At the same time, the spatial resolution of the systems dramatically improves with a shorter imaging distance.

Two different approaches are perceived for using ETACT in scintimammography. One is

imaging the entire breast or axillary region looking for tumors or involved lymph nodes. In this case the entire region would be imaged. For example the entire breast would need to be within the field of view. The other is that a feature has been deemed suspicious according to some other modality (say the mammogram) and we are only interested in imaging that small region to determine whether there is any uptake of the radiotracer. In both of these cases we would like to image at as small a distance as possible. However, currently, we are limited by the necessity of including the markers in each image. If we could devise a method for imaging the markers that did not put the geometric constraints of imaging distance on the system, then we should be able to acquire substantially better data than indicated in our preliminary study. In addition, the markers in the radionuclide image appear very similar to the feature of interest (tumors). Both are small, hot features on the image. If a marker is very hot compared to the tumor, it can make the tumor difficult to discern. This ambiguity can potentially limit the effectiveness of the ETACT approach. If we could utilize a marker system that was not radioactive, it could alleviate this problem.

For these reasons, we are investigating the use of an optical sensor, calibrated to the nuclear imager, for imaging the markers. Our prototype will consist of a digital optical camera that is mounted rigidly to the gamma camera head. A calibration scheme will be developed in order to map the location of the optical markers onto the radionuclide image. The radionuclide projection images as well as the optical images of the breast will be acquired simultaneously with the gamma camera as close as necessary to image the region of interest. The locations of the optical markers will then be mapped onto the radionuclide projection image space and the ETACT reconstruction algorithm will be applied. We expect that this approach will yield a substantial improvement in image quality and will eliminate the ambiguity introduced by the presence of the markers in the radionuclide image.

VII. Review of Statement of Work

In this section, we will review the original statement of work and review the status of each component. The review on current status for each step will be in square brackets [] and italicized so that it will be easily distinguishable from the original task.

Task 1: To develop and utilize a computer simulation model (Months 1-15) [*new estimate is Months 1-30*]

- Develop female, thoracic computer phantom including breasts, tumor, lymph nodes, heart, liver and lungs [*This has been completed.*]
- Model radiologic properties of phantom including emission, detection, attenuation, scatter and Poisson noise [*We have modeled emission, detection and Poisson noise. Modeling of attenuation and scatter will be complete in Months 24-27*]
- Model ETACT with number of fiducial markers, placement of markers, number and orientation of ETACT views [*This has been completed*]
- Model conventional SMM including both planar and SPECT [*This has been completed*]
- Run simulations varying lesion size, location and T/NT ratio [*This has been completed for aperture size. We will study the number of projections and angular disparity in Months 24-27.*]
- Determine SNR and perform ROC analysis to compare different ETACT configurations to each other and to conventional SMM [*This will be done in Months 24-30*]

Task 2: To acquire and utilize phantom data to further compare ETACT to conventional SMM (*New estimate Months 6-36*)

- Develop phantom protocol including lesion placement, size and T/NT ratio and activity in other organs (heart, liver and chest) [*This has been completed*]
- Acquire ETACT data with portable gamma camera and pinhole collimator varying number and location of fiducial markers, number and location of views and reconstruction method [*This has been completed*]
- Acquire conventional SMM including planar and SPECT [*We have acquired the planar data. Wee will acquire the SPECT data in Months 27-30*]
- Perform ROI analysis to determine the SNR in the phantom data [*This will be done in Months 24-30*]
- Perform ROC analysis to compare different implementations of ETACT to each other and to conventional SMM [*This will be done in Months 30-36*]

Task 3: To design a clinical ETACT scintimammographic system prototype (Months 24-36)

- Based on results of Tasks 1 and 2, design the optimal, acquisition parameters for ETACT SMM [*This will be done in Months 27-33*]
- Design a system for reliable and practical method of marker placement [*This will be done in Months 24-33*]
- Review design with both technical and physician staff in both nuclear medicine and mammography [*This will be done in Months 33-36*]
- Modify and finalize design based on clinical feedback. [*This will be done in Months 33-36*]

Key Research Accomplishments

Task 1: To develop and utilize a computer simulation model

- We have developed a 3D tool for simulating the ETACT acquisition process including emission, pinhole collimation, detection and Poisson noise.
- We have developed a simple breast tumor model for the evaluation of scintimammography.
- We have migrated this application from SGI to NT to make it more accessible.
- We have performed a evaluation of the aperture size using the simulation application described above.

Task 2: To acquire and utilize phantom data to further compare ETACT to conventional SMM

- We have acquired the Data Spectrum breast phantom and have developed a protocol for imaging this phantom with fiducial markers using a portable gamma camera with a pinhole collimator.
- We have acquired a preliminary comparison between ETACT and planar SMM using phantom data.
- We have validated our simulation results and shown ETACT to be a clinically practical approach.

Reportable Outcomes

Fahey FH, Webber RL, Harkness BA. ETACT: a novel approach to scintimammography. J Nucl Med 1998; 39:24P (abstract, presented at the Society of Nuclear Medicine Annual Meeting, Toronto, June 1998)

Fahey FH, Webber RL, Bayram E, Harkness BA, Mu Z, Hemler P. Preliminary Evaluation of ETACT Scintimammography. Med Phys 1999; 26:1072 (abstract, presented at the American Association of Physicists in Medicine Annual Meeting, Nashville, July 1999)

Hemler PF, Webber RL, Fahey FH. Modeling and error identification of three dimensional tomosynthesis reconstructions. SPIE Proceedings. 2000;3979:1280-1287 (presented at the SPIE Symposium on Medical Imaging, February 2000)

Fahey FH, Grow KL, Webber RL, Bayram E, Harkness BA, Hemler PF. ETACT: A Novel Approach to Scintimammography. ERA of Hope Proceedings, Vol 1. 2000. (abstract, presented at the Era of Hope Meeting, Atlanta, June 2000)

Grow KL. Evaluation of Emission Tuned Aperture Computed Tomography. Masters Thesis. Wake Forest University, 2000.

Conclusions

We have implemented the ETACT reconstruction algorithm that we described in our application. We have further developed a computerized simulation model for the acquisition process associated with ETACT including emission, collimation, detection and Poisson noise and migrated it from SGI to NT. We have also developed a simple model for the breast with a small tumor which also includes the fiducial markers necessary for doing ETACT. We used these simulation tools to perform an evaluation of the aperture size appropriate for ETACT. Based on this evaluation, it was determined that a 3 mm diameter aperture was optimal for ETACT, given the use of a portable gamma camera with a pinhole collimator and using radioactive markers. In addition, we obtained the Data Spectrum breast phantom with tumor inserts and developed a technique for creating adequate radioactive fiducial markers and for acquiring pinhole projections of the phantom. Using this phantom, we performed a preliminary evaluation to test the validity of our simulations and the feasibility of this approach. {Enter specific conclusions} Both of these evaluations indicated that we need to greatly reduce the aperture-to-object distance if we are to improve the performance of ETACT. In order to accomplish this, we will investigate the use of optical fiducial markers with a digital camera.

In the next year, we will further develop a female, thoracic phantom that includes breasts, tumors, lymph nodes, heart, lungs, and liver. We will then simulate ETACT projection data so as to evaluate projection number and angular divergence as a function of tumor size, location and T/NT ratio. We will compare ETACT to SMM and SPECT using these simulated results. We will further develop a methodology for acquiring ETACT data using optical markers. Once developed, we will acquire additional phantom data that will evaluate tumor size and location, the effect of cardiac or liver activity and compare the results to SMM and SPECT. We will continue to evaluate ETACT through these phantom experiments and will develop a clinical prototype of this method with feedback from both nuclear medicine and breast imaging physicians.

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Grant DG, Tomosynthesis: A three-dimensional radiographic imaging technique. IEEE Trans Biomed Engin 1972; BME-19:20-28.

Webber RL, Horton RA, Tyndall DA, Ludlow JB. Tuned-aperture computed tomography (TACT^{TM}). Theory and application for three-dimensional dento-alveolar imaging. Dentomaxill Radiol 1997; 26:53-62.

Appendix

This appendix includes the figures from the *Body of the Report*.

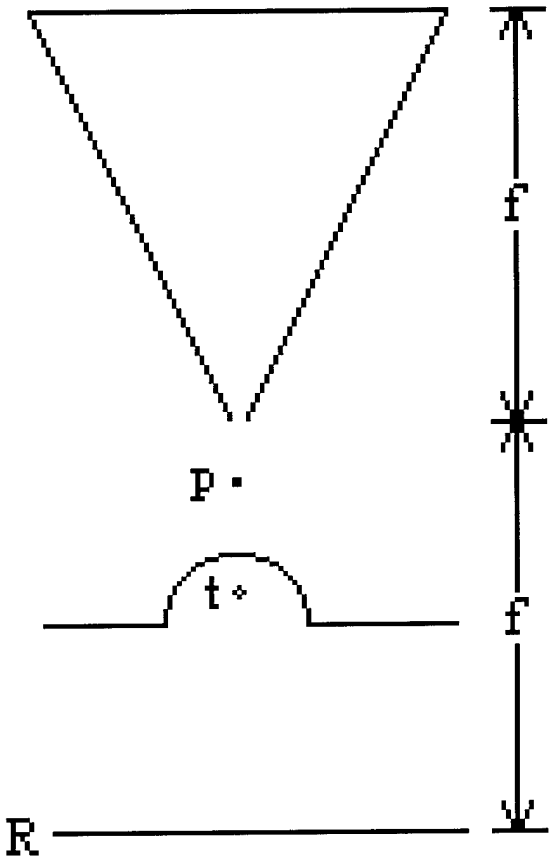

Figure 1. ETACT. The gamma camera with a conical, pinhole collimator is shown on the left. The detector plane is at the top. The reference plane (marked "R") is the same distance (f) from the pinhole aperture as the detector plane. The fiducial marker and tumor are marked with a p and t, respectively.

Figure 2. One projection through the simulated object. The tumor and the 5 fiducial markers are easily visible. Seven projections were generated at different angles which were subsequently blurred and noise was added depending on the pinhole aperture being simulated.

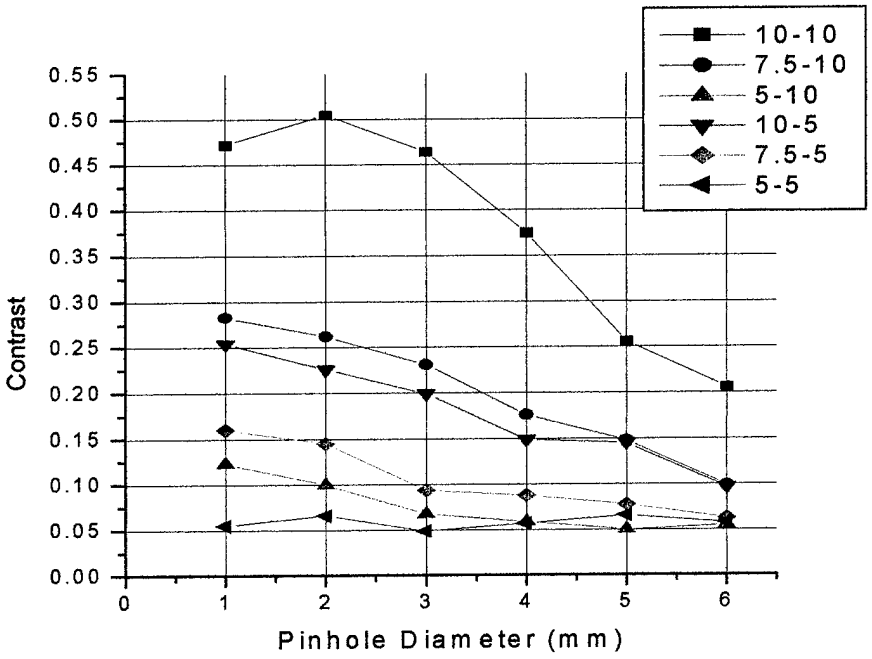

Figure 3. Simulated Results. Contrast versus pinhole diameter. Contrast improves with smaller pinhole diameter due to increased spatial resolution and thus less partial volume effect.

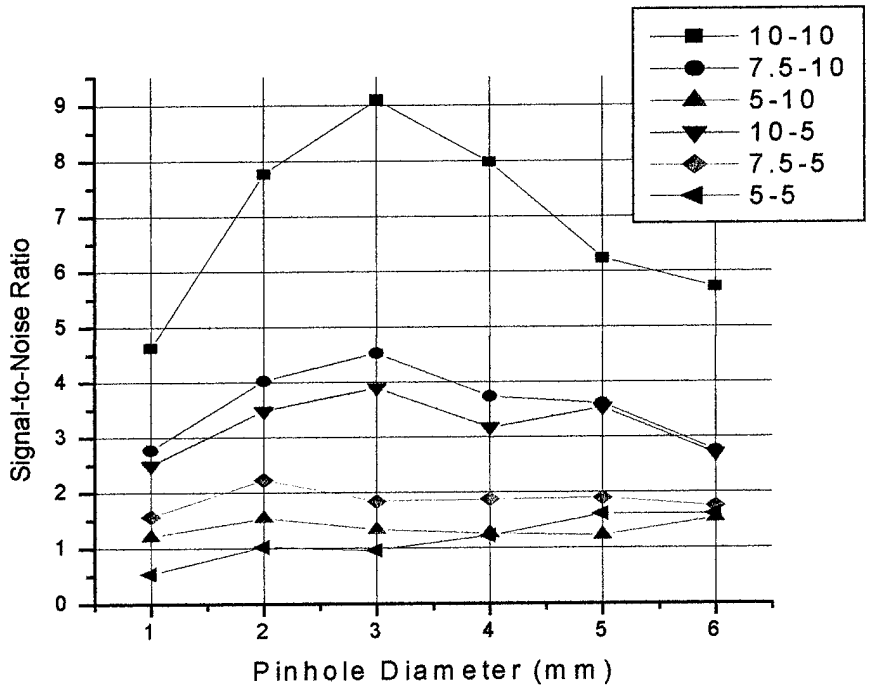

Figure 4. Simulated Results – SNR versus pinhole diameter. Small pinhole diameters lead to noisy images whereas large diameters lead to blurry images. The 3mm pinhole diameter appears to be optimum.

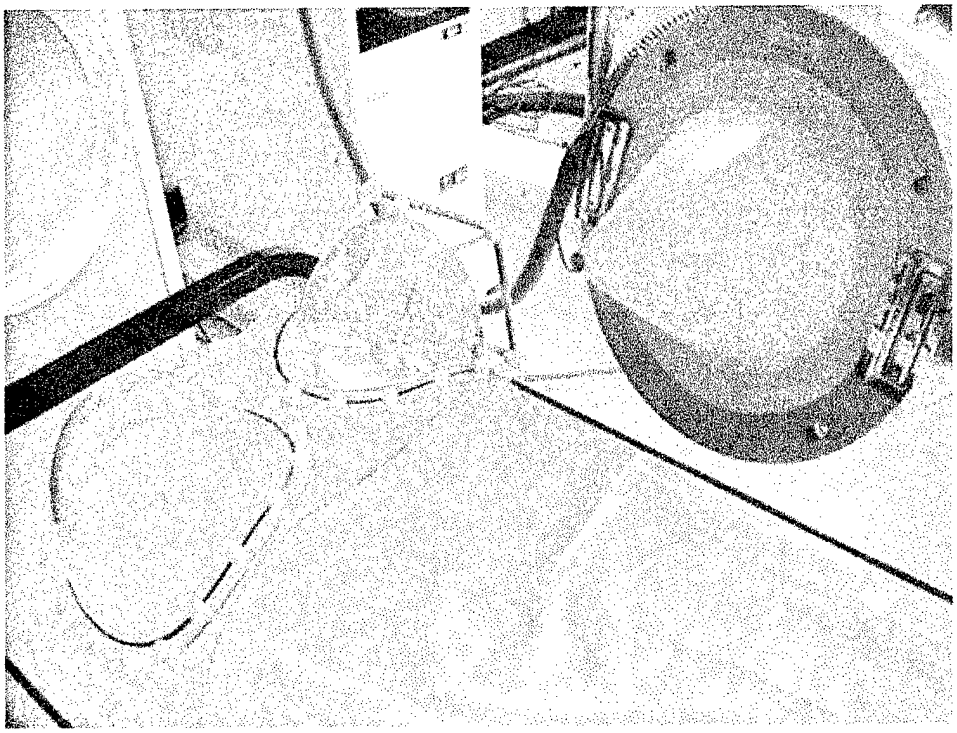

Figure 5. Phantom Experiment Setup. The Data Spectrum breast phantom is shown with the tumor in place and the plastic frame holding the fiducial markers. The gamma camera with the pinhole collimator is also shown.

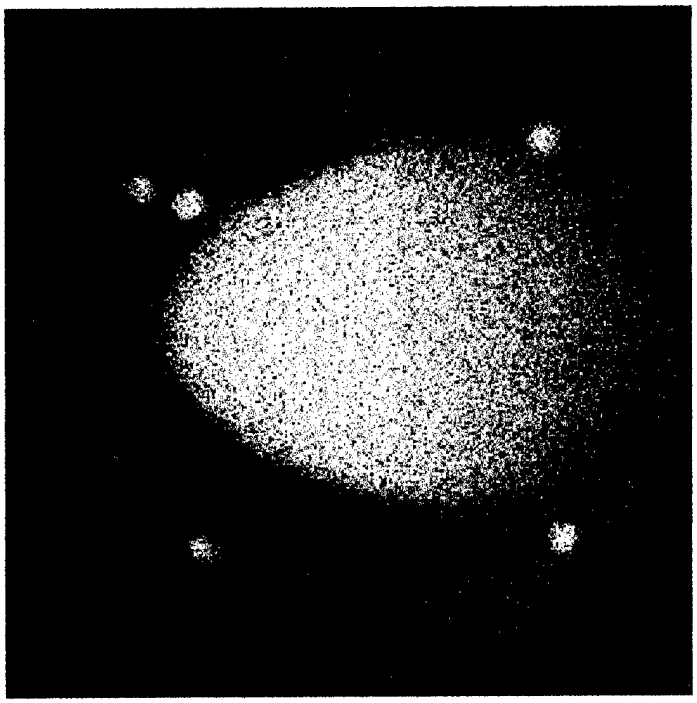

Figure 6. One projection through the phantom. The 5 fiducial markers are clearly visible. The tumor is barely visible.